Injection Therapy for the Management of Superficial Subcutaneous Lipomas

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ABSTRACT

Superficial subcutaneous lipomas are common benign tumors of the subcutaneous adipose tissue. Removal of superficial subcutaneous lipomas is achieved with simple surgical excision for the purposes of improved cosmesis, removing painful lipomas, or for the removal of a lipoma affecting function through mass effect. As research in localized fat reduction has improved, therapies successful in this domain have been applied to the management of lipomas as a surgical alternative. In this review article, the authors review the basic science of injection therapies used in the management of lipomas as well as their potential efficacy and limitations. (*J Clin Aesthet Dermatol.* 2014;7(6):46–48.)

Superficial subcutaneous lipomas are common benign tumors that most commonly occur in the subcutaneous adipose tissue of the back, neck, and proximal extremities.[1] Though surgical excision remains the primary therapy for the treatment of lipomas, newer nonsurgical alternatives have been increasingly studied to prevent some of the deformities and scarring common in surgical excision.[2] The authors review scientific advancements in injection lipolysis as it pertains to superficial subcutaneous lipoma management.

INJECTIONS

Phosphatidyl choline (PDC) is a cell membrane component that is prepared as a solubilized, injectable formulation given with deoxycholate (DC), a bile acid.[3] Prior to its experimental use in treating lipomas, PDC/DC preparations had been used for cosmetic reductions of local fat deposits.[4] Due to the similar composition between these fatty tissues, injection therapy was experimentally applied to the management of lipomas.

PDC injected in adipose was found to induce the formation of liposomes from fat molecules contained within local adipocytes, with DC forming micelles.[4] The micelles could subsequently be cleared from the body with the end effect of localized fat reduction.[5] It has also been proposed that PDC acts as both an emulsifier and as a stimulator of lipase.[6]

Prior to its utilization in the treatment of fat deposits and lipomas, PDC had been studied for prevention and treatment of various metabolic abnormalities, including hypercholesterolemia and plaque buildup in vessels.[7,8] Its efficacy in the treatment of these conditions ultimately lead to its trial in the treatment of localized fat deposits. However, in order to solubilize the solid PDC to an injectable form, DC was added.[9] As a result, the majority of studies analyzing PDC's efficacy in fat reduction have included DC. Recent studies, however, have indicated that DC may be the only "essential" or active component in this combination.[10]

Rotunda et al studied the effects of lone DC on lipomas as a standalone therapy, finding it to be equally effective at managing lipomas.[10,11] *In vitro* analysis of the PDC/DC combination demonstrated cell lysis due primarily to the detergent effects of DC. DC alone or PDC combined with DC were both found to result in similar histological changes to cultured keratinocytes, though trials with the PDC/DC combination did demonstrate marginally increased cell lysis. Both solutions likewise resulted in comparable decreases in cell viability. Thus, PDC may play a synergistic role with DC.[12]

Deoxycholate's specificity toward adipose tissue is questionable. Rotunda et al[12] demonstrated that cell lysis was not entirely limited to adipose tissue and did affect adjacent muscle. Uyger et al,[13] however, demonstrated that even with direct injection of PDC/DC into peripheral nervous tissue, there was no neuronal damage.

When injected into lipomas *in vivo*, PDC/DC causes fat necrosis. Histological evaluation of patients' tissue at various points in time after receiving injections with PDC/DC

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TABLE 1. Summary of studies assessing injection lipolysis in the management of lipomas

TREATMENT	STUDY	SITE	n	OUTCOME MEASURED	% CHANGE IN SIZE
PDC/DC	Bechara et al[16]	Dermal lipoma	30	Cross-sectional surface	45.8% decrease
DC	Rotunda et al[10]	Dermal lipoma	12	Surface area	75% decrease
PDC/DC	Kopera et al[17]	Dermal lipoma	19	Volume	44% decrease in 13/19 41% increase in 6/19
Steroid + β2 agonist	Redman et al[21]	Dermal lipoma	10	Volume	50% decrease

PDC=phosphatidyl choline; DC=deoxycholate

demonstrated various cellular changes.[14] Four hours following injection into the lipoma, the adipocyte was found to decrease in size and alter its shape focally around injected areas. Additionally, the tissue demonstrated supparative panniculitis, which progressed to a predominantly neutrophilic inflammation over the course of 48 hours with an ultimate progression toward an inflammation characterized by lymphocytes and macrophages. After 10 days following injection into the lipoma, lipophages were found to be present within the tissue. Thirty and 60 days removed from the injection, the tissue was devoid of neutrophils, but still exhibited a lymphocytic inflammation with large lipophages. Additionally, the lipoma was observed to exhibit a broadened capsule, which reportedly improved the surgeons' ability to resect the mass. A separate study examining the histology 12 weeks following the injection noted lipomatous tissue with focal fibrosis as well as foamy histiocytes, pseudomembranous degeneration of the fat tissue, and a granulomatous reaction.[15]

Injections have demonstrated size reductions ranging from 37 percent to complete resolution of the lipoma. One study, however, demonstrated a mean reduction in size by 44 percent in 13 of 19 lipomas, but paradoxically, a mean increase in size of 41 percent in the other six.[16,17] Full recurrence of a lipoma thought to be completely treated has been reported.[18] Thus, long-term studies of recurrence are necessary to better determine the efficacy of these injections as a stand-alone therapy.

Studies of both lipoma reduction and localized fat reduction using PDC/DC demonstrate similar adverse side-effect profiles. Hexsel et al[4] noted that some patients had bruising, erythema, edema, and pruritis at the treated sites. These side effects, however, resolved without complication. Additionally, recent pharmokinetic studies of injected deoxycholate demonstrate a transient increase of serum deoxycholate concentration with no alterations in serum triglycerides, lipids, or cholesterol.[19]

While the use of PDC/DC appears to be a promising therapy to reduce total lipoma size, there are certain limitations.[20] Though rare, liposarcoma must be ruled out, especially on masses of the distal extremity where liposarcomas are more common.[21] Additionally, due to DC's ability to cause potentially nonspecific cell lysis, the clinician must use caution injecting PDC/DC in proximity to tendons and muscles.[22] Additionally, as PDC/DC has not been approved by the United States Food and Drug Administration and many other international bodies as an active ingredient for any indication including lipolysis, there remains much uncertainty regarding long-term safety. Lastly, should lipomas return, surgical excision may become more difficult due to fibrosis and alterations of the lipoma capsule. Thus, further studies are necessary to address these issues.

Besides PDC/DC, β2 adrenergic agonists combined with corticosteroids have been shown in a study to be efficacious at reducing the size of lipomas.[22] Isoproterenol, a non-selective β adrenergic agonist given as a subcutaneous injection, was found to cause localized fat reduction without causing systemic toxicity, likely by stimulating lipolysis.[23] Subsequent downregulation of the β2 adrenergic receptor, however, causes decreased lipid breakdown products, suggesting the β2 receptor's more dominant role in this fat reduction.[24]

Corticosteroids, in addition to their ability to directly induce lipolysis,[25] have been found to prevent the downregulation of β2 adrenergic receptors by increasing the total quantity of receptors.[26,27] When injected into a lipoma, subsequent size reduction was found to average 50 percent.[22] Following the cessation of therapy after four weeks, however, the lipomas began to increase in size again. Patients in this study elected to have their lipomas removed and histological examination demonstrated a normal lipoma tissue architecture. Thus, while this therapy appears limited in its ability to prevent surgery, it can serve as a preoperative treatment to reduce the surgical incision size, especially due to the lack of fibrosis and cellular changes caused by this

therapy. The effect of the corticosteroids on the subsequent healing could, however, limit this method's effectiveness. A summary of studies assessing lipoma injections is provided in Table 1.

CONCLUSION

While lipolytic injections appear to be a moderately effective therapy for the removal of superficial subcutaneous lipomas, there is a lack of long-term studies assessing efficacy, safety, and recurrence. A Phase 2 trial of deoxycholate injections in superficial lipomas (NCT-00608842, ClinicalTrials.gov) will provide significant information in this regard. The ease of post-injection surgical removal must also be considered. Due to high recurrence rates seen in current studies, a presurgical reduction in the size of the lipoma with a subsequently smaller wound site could improve postsurgical cosmesis as well as facilitate the removal of large lipomas in surgically challenging locations. Fibrosis, changes in the lipoma capsule, and alterations in surrounding fat could, however, make this removal in fact more difficult. β2 adrenergic agonists combined with corticosteroid could avoid this fibrosis by maintaining the lipoma's architecture and avoiding inflammation. Additional studies are thus necessary to better understand preoperative injection therapy's effect on wound healing and any subsequent surgical excision.

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